DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

JUL 6 2006

WARNING LETTER

VIA FEDERAL EXPRESS

Myron B. Stachniw, M.D.
Galesburg Orthopedic Services, Ltd.
834 N. Seminary Street, Suite 102
Galesburg, IL 61401

Dear Dr. Stachniw:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at your clinical site from March 20 through April 5, 2006, by an investigator from the FDA Chicago District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the clinical studies [redacted] Safety and Efficacy Study of the [redacted] are devices as that term is defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 321(h). This letter also requests prompt corrective action to address the violations cited and discusses your written response to the noted violations.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval (PMA) applications, and Premarket Notification submissions (510(k)) are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 C.F.R.) Part 812 -- Investigational Device Exemptions, and Part 50 -- Protection of Human Subjects. At the close of the inspection, the FDA investigator presented an inspectional observations form FDA 483 for your review and discussed the observations listed on the form with you. The deviations noted on the FDA 483, your written response, and our subsequent review of the inspection report are discussed below:

Failure to obtain FDA and Institutional Review Board approval prior to allowing subjects to participate in a study. [21 CFR 812.110(a)]

An investigator may determine whether potential subjects would be interested in participating in an investigation, but shall not request the written informed consent of any subject to participate, and shall not allow any subject to participate before obtaining FDA and IRB approval. You allowed subjects to participate in the [redacted] study prior to receiving FDA and IRB approval. The FDA approval date for the Investigational Device Exemption (IDE) for the [redacted] study was March 26, 2004 and the initial IRB approval date for the [redacted] study was February 6, 2004. However, you began implanting subjects on March 12, 2003. Examples of subjects implanted prior to FDA and IRB approval include, but are not limited to, the following:

[redacted]

Subject ID	Date of Implantation	Date of IRB Approval	FDA IDE Approval Date
[redacted]	11/11/03	2/6/04	3/26/04
	11/19/03	2/6/04	3/26/04
	12/31/03	2/6/04	3/26/04
	1/30/04	2/6/04	3/26/04
	3/12/03	2/6/04	3/26/04
	5/8/03	2/6/04	3/26/04

In your written response to the inspectional observations, dated April 12, 2006, you state that you have developed a regulatory status checklist to help study staff determine the regulatory status of a device. Please submit a copy of the checklist and the new procedures referenced in your response with the associated implementation dates.

Failure to obtain proper informed consent prior to any study related procedures. [21 CFR 812.100 and 21 CFR 50.20]

Investigators are responsible for ensuring that informed consent is obtained from a subject or the subject's legally authorized representative prior to initiation of any study-related procedures. You failed to comply with the above-stated regulations for the [redacted] studies. Examples of this failure include, but are not limited to, the following:

[redacted]

Subject ID	Date Device Implanted	Date Informed Consent Signed
[redacted]	7/22/03	7/30/04
	12/31/03	11/17/05

[redacted]

Subject ID	Date Device Implanted	Date Informed Consent Signed
[redacted]	11/11/03	11/21/05
	11/19/03	3/13/06
	12/31/03	11/17/05
	1/30/04	11/15/05
	3/29/05	2/26/06
	3/12/03	2/25/06

In your response you acknowledge your failure to obtain written consent from the aforementioned subjects prior to implanting the study devices. You state that after becoming aware of this deficiency, during a monitoring visit in November 2005, you contacted the subjects who had not been consented, explained the risks associated with the study device, and obtained written informed consent. This corrective action appears to be adequate.

In addition, you indicate that you will utilize a preoperative worksheet, to be completed prior to surgery, to confirm informed consent is obtained prior to surgery. Please be aware that informed consent must be obtained prior to the initiation of any study related procedures which includes study procedures completed prior to surgery.

Failure to notify the IRB within 5 working days after subjects received an investigational device without first signing an informed consent document. [21 CFR 812.150(a)(5)]

You failed to submit a report to the IRB within 5 working days when subjects on the [redacted] studies were implanted with the study devices without first signing an informed consent document. Examples of this failure include but are not limited to the following:

[redacted]

Subject ID	Date of Implantation	Date Informed Consent Signed	Date IRB Notified
[redacted]	7/22/03	7/30/04	2/17/06
	12/31/03	11/17/05	3/17/06

[redacted]

Subject ID	Date of Implantation	Date Informed Consent Signed	Date IRB Notified
[redacted]	4/15/04	11/15/05	3/20/06

Subsequent reporting to the IRB of the use of investigational devices without obtaining informed consent appears to be an adequate corrective action. You state in your response that you will also implement the use of the preoperative worksheet, procedures on documenting and filing signed informed consent forms, and procedures which outline a

clinical investigator's reporting responsibilities under the FDA regulations. Please provide a copy of the procedures on documenting and filing signed informed consent forms.

Failure to ensure an investigation is conducted in accordance with the signed agreement, the investigational plan, applicable FDA regulations and any conditions of approval imposed by the FDA or the IRB. [21 CFR 812.110(b)]

As a clinical investigator it is your responsibility to conduct the clinical investigation in accordance with the signed investigator agreement, investigational plan, applicable FDA regulations, and any conditions of approval imposed by FDA or the IRB. You failed to adhere to this regulation. Examples of this failure include, but are not limited to, the following:

1. [redacted] <70 points is required as an inclusion criteria in the [redacted] were not documented to support eligibility for any of the subjects participating in either study.

In your response, you state that you will certify and document that the [redacted] Scores are accurate for the subjects already enrolled on both studies. Your response appears to be an adequate corrective action plan. In addition, you stated that you have developed procedures outlining the requirements for conducting a study in accordance with a clinical protocol. Please provide a copy of these procedures and the associated training documentation.

2. The protocol revision for the [redacted] study dated 6/25/04 was not submitted to the IRB for review until 3/28/06. The inspection also revealed that protocol revisions for the [redacted] study dated 2/5/01, 6/8/01, 8/22/01, and 12/10/01 had not been submitted to the IRB, and the protocol revision dated 3/24/03 was not submitted to the IRB for review until 2/17/06.

In your response, you state you will submit the [redacted] revisions to the IRB and anticipate approval in May. In addition, you state procedures will be developed outlining the requirements of obtaining IRB approval and you will submit all subsequent protocol revisions to the IRB when they are received. Please provide documentation of the [redacted] protocol revision submission to the IRB and provide a copy of the aforementioned procedures and the associated training records.

[redacted]

3. The protocol specified that radiographic measurements on x-rays were to be performed at the following intervals: preoperative, 6 weeks, 6 months, 1 year, and at 2 years. None of the measurements were completed on any of the subjects.

In your response, you state that the case report forms provided by the sponsor lacked data fields relating to radiographic assessment and that the sponsor instructed you to forward all radiographic data to the sponsor for review. You also told our investigator

that the sponsor informed you the protocol would be revised to relieve you of the responsibility to perform these measurements. However, the protocol was not amended to reflect this change and, therefore, the measurements were required. Your response is inadequate in that you have not provided a corrective action plan explaining how you will prevent the recurrence of this type of violation in the future.

[redacted]

4. Exclusion criteria for the [redacted] protocol includes subjects who have had ipsilateral [redacted] of any kind. Subjects [redacted] all met the aforementioned exclusion criteria; however, they nonetheless were enrolled in the [redacted] study.

In your response, you acknowledge that patients meeting the exclusion criteria of the protocol were treated under the [redacted] study. Your response to this violation is inadequate in that you have not presented a plan to prevent ineligible subjects from entering a research study. Please provide a plan to prevent ineligible subjects (not including subjects treated under the Expanded Access Mechanisms) from entering a research study.

Failure to submit complete, accurate, and timely reports. [21 CFR 812.150(a)(3)]

An investigator shall submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly. You failed to adhere to this regulation in that you did not submit complete, accurate, and timely progress reports to the IRB for the [redacted] study. The study received initial IRB approval on 2/6/04; however, a request for continuing review was not submitted to the IRB until 3/28/06.

In your response, you state verbal updates were provided to the IRB in the past but documentation of the verbal updates was not maintained. You further state that two written progress reports, dated March 6 and March 20, 2006, were submitted to the IRB. Please provide copies of these IRB progress reports. In addition, you state that you are developing procedures outlining the reporting requirements and suggested content for the progress reports. Please provide a copy of the procedures and the associated training documentation when these steps have been completed.

Failure to limit the use of an investigational device to subjects under the investigator's supervision. Failure to limit supply of an investigational device only to authorized persons. [21 CFR 812.110(c)]

Investigational devices were implanted in three subjects by a physician who was not under your direct supervision; nor had the physician signed a clinical agreement with the sponsor at the time of implantation. Therefore, the physician was not authorized to receive the device. Examples of this failure include, but are not limited to the following:

[redacted]

Subject ID	Date of Implantation	Date Investigator Agreement Signed
[redacted]	11/19/03	1/11/06
	12/31/03	1/11/06
	01/30/04	1/11/06

In your response, you state that copies of all signed investigator agreements will be maintained and stored in the regulatory binder. In addition, you state that because you are the only person allowed to sign for the receipt of investigational inventory, you will be able to control the release of the investigational devices. These steps appear to be adequate to prevent this violation from occurring again in the future.

Failure to maintain accurate, complete, and current records regarding the receipt, use, or disposition of a study device [21 CFR 812.140(a)(2)]

An investigator is responsible for maintaining records of the names of all persons who received, used, or disposed of each device, as well as records relating to why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of. You failed to maintain accurate, complete, and current records regarding the receipt, use, or disposition of devices used in the [redacted] studies, including documentation regarding the return of unused devices and the disposition of explanted devices. Examples of this failure include, but are not limited to the following:

[redacted]

Lot numbers for all [redacted] devices have not been identified. In addition, device accountability records for subject [redacted] indicate the [redacted] lot [redacted] and [redacted] were utilized but no order/consignment packing list was found for either component.

[redacted]

With regard to the [redacted] Study, the inspection revealed that your site lacked device delivery records, order/consignment packing slips, invoices, product order forms, and other records relating to product usage and disposition.

In your response, you state that you decided to suspend enrollment in the [redacted] studies until you are able to correct the problems relating to poor inventory documentation at your site. You also describe how you were able to recreate an investigational inventory log which accurately reflects device usage, explants, and discarded devices for both studies. In addition, you state that you and other study personnel received training on new device handling procedures developed by the study sponsor, and you further indicate that you have developed a device accountability log that is designed to track the receipt and disposition of each investigational device.

Training for handling procedures developed by the sponsor and development of the device accountability log appear to be adequate steps to potentially prevent this violation

from occurring again in the future. Please provide a copy of the investigational inventory logs you completed for the [redacted] studies.

The violations described above are not intended to be an all inclusive list of problems that may exist with your clinical study. It is your responsibility as a clinical investigator to ensure compliance with the Act and applicable regulations. Suspending enrollment for both studies was an appropriate step to take while you assess your program for compliance issues.

Within fifteen (15) working days of receiving this letter, please provide written documentation of the additional actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the clinical investigator. In addition, please provide a complete list of all clinical trials in which you have participated for the last five years, including the name of the study and test article, the name of the sponsor, the number of subjects enrolled, and the current status of the study. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. In addition, FDA could initiate disqualification proceedings against you in accordance with 21 C.F.R. 812.119.

You will find information to assist you in understanding your responsibilities and planning your corrective actions in the FDA Information Sheets Guidance for Institutional Review Boards and Clinical Investigators, which can be found at http://www.fda.gov/oc/ohrt/irbs/. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Send your response to: Attention: Doreen Kezer, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 9200 Corporate Boulevard, HFZ-310, Rockville, Maryland 20850.

A copy of this letter has been sent to the Chicago District Office, 550 W. Jackson, Suite 1500, Chicago, IL 60661. Please send a copy of your response to that office.

If you have any questions, please contact Doreen Kezer, 240-276-0125, doreen.kezer@fda.hhs.gov.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and Radiological Health